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## Multicenter evaluation of dynamic three-dimensional magnetic resonance myocardial perfusion imaging for the detection of coronary artery disease defined by fractional flow reserve

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**Abstract:** BACKGROUND First-pass myocardial perfusion cardiovascular magnetic resonance (CMR) imaging yields high diagnostic accuracy for the detection of coronary artery disease (CAD). However, standard 2D multislice CMR perfusion techniques provide only limited cardiac coverage, and hence considerable assumptions are required to assess myocardial ischemic burden. The aim of this prospective study was to assess the diagnostic performance of 3D myocardial perfusion CMR to detect functionally relevant CAD with fractional flow reserve (FFR) as a reference standard in a multicenter setting. **METHODS AND RESULTS** A total of 155 patients with suspected CAD listed for coronary angiography with FFR were prospectively enrolled from 5 European centers. 3D perfusion CMR was acquired on 3T MR systems from a single vendor under adenosine stress and at rest. All CMR perfusion analyses were performed in a central laboratory and blinded to all clinical data. One hundred fifty patients were successfully examined (mean age  $62.9 \pm 10$  years, 45 female). The prevalence of CAD defined by FFR ( $<0.8$ ) was 56.7% (85 of 150 patients). The sensitivity and specificity of 3D perfusion CMR were 84.7% and 90.8% relative to the FFR reference. Comparison to quantitative coronary angiography (50%) yielded a prevalence of 65.3%, sensitivity and specificity of 76.5% and 94.2%, respectively. **CONCLUSIONS** In this multicenter study, 3D myocardial perfusion CMR proved highly diagnostic for the detection of significant CAD as defined by FFR.

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## Multicenter Evaluation of Dynamic Three-Dimensional Magnetic Resonance Myocardial Perfusion Imaging for the Detection of Coronary Artery Disease Defined by Fractional Flow Reserve

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Christiane Kuhl, MD; Eike Nagel, MD, PhD; Eckart Fleck, MD; Nikolaus Marx, MD;  
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**Background**—First-pass myocardial perfusion cardiovascular magnetic resonance (CMR) imaging yields high diagnostic accuracy for the detection of coronary artery disease (CAD). However, standard 2D multislice CMR perfusion techniques provide only limited cardiac coverage, and hence considerable assumptions are required to assess myocardial ischemic burden. The aim of this prospective study was to assess the diagnostic performance of 3D myocardial perfusion CMR to detect functionally relevant CAD with fractional flow reserve (FFR) as a reference standard in a multicenter setting.

**Methods and Results**—A total of 155 patients with suspected CAD listed for coronary angiography with FFR were prospectively enrolled from 5 European centers. 3D perfusion CMR was acquired on 3T MR systems from a single vendor under adenosine stress and at rest. All CMR perfusion analyses were performed in a central laboratory and blinded to all clinical data. One hundred fifty patients were successfully examined (mean age  $62.9 \pm 10$  years, 45 female). The prevalence of CAD defined by FFR ( $<0.8$ ) was 56.7% (85 of 150 patients). The sensitivity and specificity of 3D perfusion CMR were 84.7% and 90.8% relative to the FFR reference. Comparison to quantitative coronary angiography ( $\geq 50\%$ ) yielded a prevalence of 65.3%, sensitivity and specificity of 76.5% and 94.2%, respectively.

**Conclusions**—In this multicenter study, 3D myocardial perfusion CMR proved highly diagnostic for the detection of significant CAD as defined by FFR. (*Circ Cardiovasc Imaging*. 2015;8:e003061. DOI: 10.1161/CIRCIMAGING.114.003061.)

**Key Words:** coronary artery disease ■ fractional flow reserve ■ magnetic resonance imaging  
■ myocardial perfusion ■ multicenter study

Myocardial perfusion imaging with cardiovascular magnetic resonance (CMR) yields high diagnostic accuracy for the detection of coronary artery disease (CAD),<sup>1–8</sup> and its prognostic value has also been documented.<sup>9–13</sup> Standard two-dimensional (2D) multislice perfusion CMR techniques have been compared with single photon emission computed tomography in multicenter and single center trials,<sup>2,5,7,14,15</sup> confirming the high diagnostic accuracy of CMR in prospective patient cohorts. Excellent diagnostic performance has been documented relative to hemodynamic measurements using fractional flow reserve (FFR) at 1.5 T in a single center setting.<sup>16</sup> A potential limitation of standard 2D techniques, however, relates to the limited spatial coverage, which requires geometric assumptions for the quantification of ischemic tissue volume to guide therapy as recommended by the recent European guidelines on myocardial revascularization.<sup>17</sup> Compared with

methods that cover the whole heart, the acquisition of a limited number of slices may also affect the diagnostic performance as has been indicated previously by comparing 3D versus simulated 3-slice 2D perfusion imaging.<sup>18</sup>

### See Clinical Perspective

To address the limited, noncontiguous coverage of 2D multislice myocardial perfusion CMR techniques, three-dimensional (3D) methods have been developed based on recent advances in CMR scan acceleration methodology.<sup>19,20</sup> Whole-heart coverage is achieved by using data undersampling strategies in conjunction with appropriate image reconstruction techniques,<sup>21</sup> such as (*k-t*) imaging, including sensitivity encoding<sup>22–24</sup> or principal component analysis.<sup>25</sup> The diagnostic accuracy of 3D perfusion CMR has recently been validated in single-center studies against both quantitative coronary angiography (QCA)<sup>18</sup> and

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FFR<sup>26</sup> in patients with known or suspected CAD. Estimates of myocardial ischemic burden (MIB) from 3D perfusion CMR have also been shown to strongly correlate with those from single photon emission computed tomography.<sup>27</sup> In addition, the high interstudy reproducibility of 3D myocardial perfusion CMR at 1.5 T has been shown in 2 different centers.<sup>28</sup>

The objective of the current study was to prospectively evaluate the diagnostic performance of dynamic whole-heart 3D myocardial perfusion CMR at 3.0 T for the detection of significant CAD as defined by FFR in a multicenter setting.

## Methods

### Study Population

The present prospective study was conducted at 5 European centers (University Hospital Zurich, Switzerland; University Hospital RWTH Aachen, Germany; German Heart Institute Berlin, Germany; King's College London, United Kingdom; University of Leeds, United Kingdom). The study was approved by the local ethics review boards and patients were prospectively enrolled upon written informed consent. Patients scheduled for diagnostic coronary angiography for the evaluation of suspected CAD were consecutively recruited between November 2011 and August 2013. Patients were instructed to refrain from caffeine-containing substances 24 hours before the examination. Exclusion criteria were standard contraindications for CMR imaging (eg, incompatible metallic implants and claustrophobia) and adenosine infusion (eg, high grade atrio-ventricular block and asthma).

### Cardiovascular Magnetic Resonance Protocol

CMR imaging was performed with the patient in the supine position using 3.0 T MR systems (Philips Healthcare, Best, The Netherlands). Depending on the actual MR scanner version, either 6-element cardiac or 28-element torso coil arrays were used for signal reception, and cardiac synchronization was performed using a vector ECG.

After the acquisition of standard cine scans for the assessment of left ventricular function, 3D myocardial perfusion CMR imaging

was planned in short-axis geometry with full left-ventricular coverage. Adenosine was administered intravenously at a dose of 140  $\mu$ g/kg/min under continuous monitoring of heart rate and blood pressure. After at least 3 minutes of adenosine infusion, stress first-pass perfusion imaging (i.v. bolus application of 0.075 mmol/kg b.w. of a gadolinium-based contrast agent, Gadovist, Bayer Healthcare, Berlin, Germany; injection rate 4.0 mL/s followed by 20 mL saline flush) was performed. After a 15-minute waiting period for equilibration of the contrast agent within the myocardium, the identical 3D myocardial perfusion CMR scan was repeated at rest. Dynamic perfusion data were acquired in every heartbeat over 30 cardiac cycles with a 3D saturation prepared spoiled turbo gradient echo sequence (repetition time/echo time/flip angle 1.8 ms/0.7 ms/15°, saturation prepulse delay 150 ms, acquisition timed to end-systole, 75% partial Fourier sampling in 2 directions, including an elliptical k-space shutter, 10 $\times$  *k-t* acquisition with 49 training profiles resulting in a net acceleration of 7 $\times$  and an acquisition window per heartbeat of 200 ms, *k-t* principal component analysis reconstruction of 16 contiguous slices of 5 mm thickness, acquired voxel size 2.3 $\times$ 2.3 mm<sup>2</sup>).<sup>20</sup> Perfusion imaging was performed during a single inspiration breathhold. Shallow expiration was permitted in case the inspiration breathhold could not be sustained during the scan. Using this approach, data acquisition in all patients suitable for CMR exams was possible.

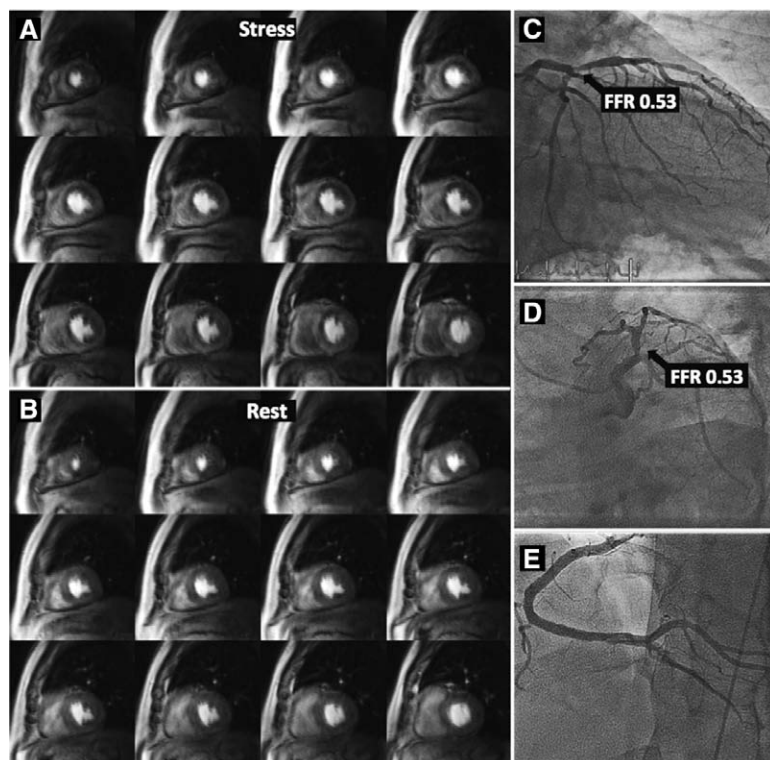
After a further 15-minute waiting period, late gadolinium enhancement imaging (0.15 mmol/kg b.w. cumulative dose) was performed in the identical short-axis geometry with a 3D inversion prepared spoiled gradient echo sequence (repetition time/echo time/flip angle 3.6 ms/1.8 ms/15°, voxel size 1.6 $\times$ 1.6 $\times$ 10 mm<sup>3</sup>). The inversion recovery prepulse delay was determined using a Look-Locker sequence and adjusted accordingly.

Sample whole-heart 3D myocardial perfusion CMR images acquired during adenosine stress and at rest are presented in Figure 1.

### Visual Assessment of Perfusion Scans

CMR images were analyzed visually in a central data analysis laboratory by reviewers blinded to clinical and angiographic patient data using a dedicated workstation (ExtendedWorkSpace, Philips Healthcare, Best, The Netherlands).

Overall image quality of stress and rest perfusion scans was graded on a scale between 1 and 4 (1=non-diagnostic, 2=poor, 3=good,



**Figure 1.** Example whole-heart 3D cardiovascular magnetic resonance (CMR) perfusion data acquired during adenosine stress (A) and at rest (B). A perfusion defect is seen in the anterior and anteroapical segments extending from base to apex. Invasive X-ray angiography confirms a relevant stenosis of the ostial left anterior descending artery with fractional flow reserve (FFR) value of 0.53. The circumflex (C,D) and right coronary artery (E) had no stenosis.



4=excellent). From all acquired image slices, the subset of short-axis slices with clearly identifiable left-ventricular cavity enhancement during contrast agent passage and with >75% circumferential left-ventricular myocardium present were identified. The selected short-axis slices were divided into 6 equally distributed circumferential segments each and evaluated visually. Perfusion defects on the stress perfusion images seen in any segment ( $\geq 1$  segment) with  $\geq 25\%$  transmural persisting for  $\geq 3$  consecutive dynamics, which were not visible in the rest perfusion scan and showed no enhancement in the late gadolinium enhancement scan, were marked to be pathological, and the overall study was considered as abnormal.

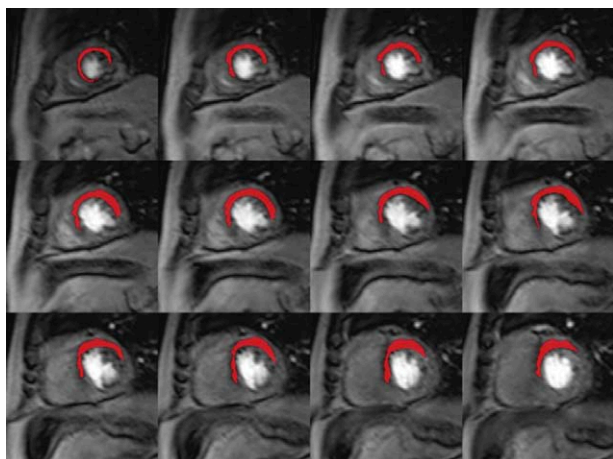
### Assessment of Myocardial Ischemic Burden

MIB was estimated based on the quantification of the tissue volume exhibiting myocardial hypo-enhancement using dedicated software (GTVolume, GyroTools LLC, Zurich, Switzerland). For determination of myocardial hypo-enhancement, the dynamic frame of the stress perfusion scan showing the maximum extent of regional hypo-enhancement during peak signal enhancement of remote myocardium was selected.<sup>18</sup> In the presence of extensive ischemia-related hypo-enhancement (eg, high grade triple vessel disease), remote myocardium either represented an entire myocardial segment or its subepicardial layer. The left ventricular endo- and epicardial borders were manually identified in all slices to determine myocardial volume. Quantification of hypo-enhanced tissue volume was performed automatically using threshold-based segmentation with a signal intensity threshold  $>2\times$  standard deviation below the signal of remote myocardium. Segmentation of myocardial hypo-enhancement during stress is illustrated in Figure 2 for the patient data shown in Figure 1.

Total volumes of left ventricular myocardium and hypo-enhanced myocardium were calculated using the disk summation method. MIB was defined by the volume of hypo-enhancement normalized to total left ventricular myocardial volume and is quoted in percentage. In case of concurrent presence of myocardial scar as identified on late gadolinium enhancement images, the amount of scar tissue volume was calculated based on segmentation of hyperintense tissue. Subsequently, the scar tissue volume was subtracted from the volume of hypo-enhancement before MIB calculation.

### Fractional Flow Reserve and Quantitative Coronary Angiography Measurements

FFR was measured using standard methods<sup>29</sup> with a 0.014-inch coronary pressure sensor–tip wire (Volcano Therapeutics, San Diego, California or Pressure-Wire Certus, St. Jude Medical Systems AB, Uppsala, Sweden) in vessels visually assessed by the angiographers as having  $\geq 50\%$  and  $\leq 80\%$  diameter stenosis in 2 orthogonal views



**Figure 2.** Segmentation of myocardial hypo-enhancement during stress for the patient data shown in Figure 1. The volume of myocardial hypo-enhancement normalized to the left ventricular volume is 37%.

with  $\geq 2$  mm luminal diameter. For the purpose of the study and in accordance to guidelines, stenoses in vessels with  $<2$  mm luminal diameter were considered nonsignificant.<sup>30</sup> Coronary stenosis with an FFR value  $<0.8$  were classified as hemodynamically relevant. Total/subtotal occlusion or high-grade stenosis ( $>80\%$  diameter stenosis) did not undergo pressure wire assessment and were considered hemodynamically significant.

Coronary angiography was performed by routine techniques. At least 2 orthogonal views of every major coronary vessel and its side branches were acquired. QCA was performed offline by an independent core laboratory being blinded to the results of CMR imaging.

### Statistical Analysis

Data analysis was performed using SPSS for Windows 17.0.0 (SPSS Inc., Chicago, IL). Data were evaluated on a patient basis to determine sensitivity, specificity, negative and positive predictive values with corresponding 95% confidence intervals (95% CI) according to standard definitions. Continuous variables are expressed as mean $\pm$ standard deviation; categorical variables are expressed as proportions. The paired Student's *t* test was used to assess the statistical significance of continuous variables between rest and stress. All tests were 2-tailed;  $P<0.05$  was considered significant. Receiver–operator characteristic curve analysis was used to determine the diagnostic accuracy (area under curve) and optimal cut-off value of MIB to detect significant CAD defined by FFR  $<0.8$ .

Cohen's kappa analysis was applied to compare 3D myocardial perfusion cardiovascular MRI outcome versus FFR outcome using the following grading: 0 to 0.2 (poor), 0.21 to 0.4 (fair), 0.41 to 0.6 (moderate), 0.61 to 0.8 (substantial), and 0.81 to 1.0 (nearly perfect).

## Results

### Patient Characteristics

The characteristics of the patient cohort are listed in Table 1. Of the 155 recruited patients, 2 studies were lost because of data storage failure, 1 study was incomplete because of patient claustrophobia, 1 study had to be terminated because of a bronchospasm during adenosine infusion and 1 study was incomplete because of an unknown ferromagnetic splint in the chest wall. Accordingly, a total of 150 patients ( $n=30$  from Zurich,  $n=30$  from Aachen,  $n=32$  from Berlin,  $n=31$  from London, and  $n=27$  from Leeds;  $n=105$  (70%) male; mean age  $62.9\pm 10.0$  years, range 33–83 years) formed the final population for analysis. Table 2 lists the hemodynamic data recorded during the CMR examination.

### Diagnostic Performance

The prevalence of CAD as defined by FFR  $<0.8$  was 56.7% (85 of 150 patients) and the sensitivity of 3D perfusion CMR was 84.7% (95% CI 75.3–91.6) with a specificity of 90.8% (95% CI 81.0–96.5) and diagnostic accuracy of 87.3% (95% CI 81.1–91.7). Positive and negative predictive values were 92.3% (95% CI 84.0–97.1) and 81.9% (95% CI 71.1–90.0), respectively.

When analyzed per vessel territory (387 of 450 territories), sensitivity was 73.5% (95% CI 63.9–81.8), specificity was 91.9% (95% CI 88.1–94.8), and diagnostic accuracy was 87.1% (95% CI 83.4–90.1). The positive predictive value was 76.5% (95% CI 66.9–84.5) and the negative predictive value was 90.7% (95% CI 86.7–93.8).

Cohen's kappa showed substantial agreement of perfusion imaging outcome and FFR outcome on a per-patient

**Table 1. Patient Demographics and Clinical Data**

Parameter	n=150
Male, n (%)	105 (70)
Age, y	62.9±10.0
Age range	33–83
BMI, kg/m <sup>2</sup>	27.8±4.3
Cardiovascular risk factors, n (%)	
Arterial hypertension	109 (73)
Diabetes mellitus	27 (18)
Hyperlipidemia	100 (67)
Smoking	73 (49)
Family history of CAD	55 (37)
Medication, n (%)	
β-Blocker	76 (51)
ACE inhibitor	71 (47)
Statin	91 (61)
Nitrates	14 (9)
Diuretics	33 (22)
ARBs	24 (16)
Ca antagonist	27 (18)
Aspirin	112 (75)
Coronary artery disease, n (%)	
Single-vessel disease	41 (27)
Multi-vessel disease	57 (38)
Left ventricular function	
LVEF (%)	62.1±7.2
LVEDV (mL)	132±36
LVESV (mL)	51±22

Data are presented as n (%) or mean±SD. ACE indicates angiotensin-converting enzyme; ARB, angiotensin-II receptor blocker; BMI, body mass index; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; and LVESV, left ventricular end-systolic volume.

and per-vessel territory analysis (kappa value 0.75 and 0.66, respectively).

The prevalence of CAD as defined by QCA ≥50% was 65.3% (98 of 150 patients). Analysis of 3D CMR perfusion data with QCA as the reference standard yielded a sensitivity

of 76.5% (95% CI 66.9–84.5), specificity of 94.2% (95% CI 84.0–98.7), and diagnostic accuracy of 82.6% (95% CI 75.8–87.9). The positive predictive value was 96.2% (95% CI 89.2–99.2) and the negative predictive value was 68.1% (95% CI 56.0–78.55).

Analysis per vessel territory relative to QCA (450 of 450 territories) yielded a sensitivity of 61.5% (95% CI 53.9–68.6), specificity of 91.5% (95% CI 87.5–94.5), and diagnostic accuracy of 79.6% (95% CI 75.6–83.0). The positive predictive value was 82.7% (95% CI 75.2–88.7) and the negative predictive value was 78.2% (95% CI 72.3–82.7).

### Myocardial Ischemic Burden

The mean MIB in all patients was 10.1%±12.2% (range, 0%–51.7%). The mean MIB in patients grouped by FFR status is given in Figure 3.

The diagnostic accuracy of MIB to detect significant CAD as defined by FFR was 0.91, and the optimal MIB cut-off value was 4.1%, which resulted in a sensitivity and specificity of 84.7% (95% CI 75.3–91.6) and 92.3% (95% CI 82.9–97.3), respectively (Figure 4).

### Image Quality

The 3D CMR stress and rest perfusion scans of all 150 patients were of diagnostic image quality (image quality score ≥2). The mean visual scores of 3D stress and rest CMR perfusion scans were 3.57±0.58 and 3.65±0.51, respectively.

### Discussion

The present multicenter study has assessed the diagnostic performance of whole-heart 3D myocardial perfusion CMR for the detection of significant CAD as determined by FFR and QCA. The main findings of the study are (1) 3D myocardial perfusion CMR at 3.0 T is a robust technique for the detection of CAD in a European multicenter, single-vendor setting; (2) the diagnostic accuracy of 3D myocardial perfusion CMR to detect functionally significant CAD is high and confirms previous data on 2D multislice and 3D whole-heart myocardial

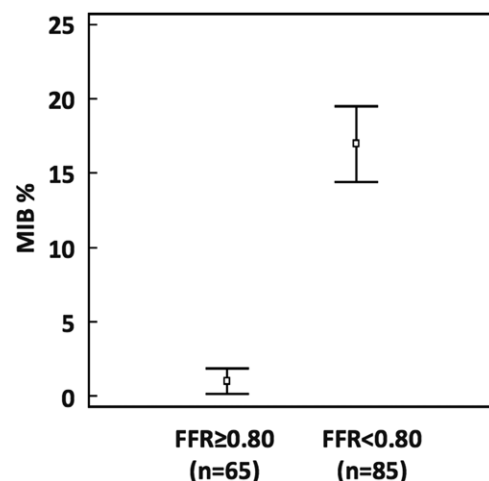
**Table 2. Hemodynamic Parameters**

Parameter	n=150
Heart rate, bpm	
At rest	65.5±12.5
Adenosine stress	83.2±15.4*
Systolic blood pressure, mm Hg	
At rest	129±21
Adenosine stress	127±21
Diastolic blood pressure, mm Hg	
At rest	73±10
Adenosine stress	71±10†

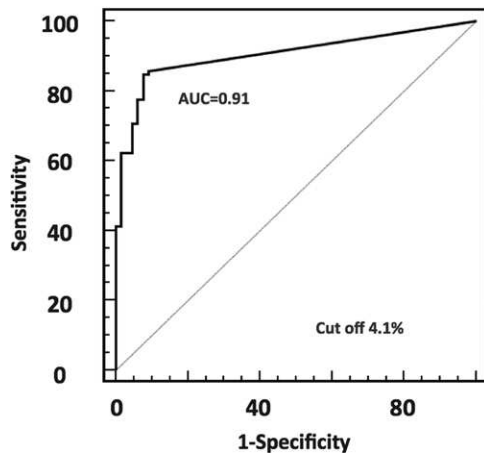
Data are presented as mean±SD.

\* $P<0.0001$ .

† $P<0.05$  for rest vs stress (paired Student's *t* test).



**Figure 3.** Myocardial ischemic burden (MIB) of the study population given as mean values and corresponding 95% confidence intervals as a function of hemodynamic stenosis significance as defined by fractional flow reserve (FFR). Differences between groups are statistically significant ( $P<0.001$ ).



**Figure 4.** Receiver–operator characteristic (ROC) analysis to determine the cut-off value of myocardial ischemic burden predictive of the presence or absence of significant coronary artery disease as defined by fractional flow reserve. A cut-off value of myocardial ischemic burden  $>4.1\%$  was found to be most significant. AUC indicates area under curve.

perfusion CMR using FFR as the reference standard<sup>16,26,28,31,32</sup>; and (3) the MIB derived from 3D whole-heart myocardial perfusion CMR provides an accurate diagnostic tool for the detection of flow-limiting CAD.

Relative to previous single-center (3T CMR) and dual-center (1.5T CMR) 3D CMR perfusion studies using FFR as a reference, our results compare well for sensitivity and specificity (85% versus 91%<sup>26</sup> versus 90%<sup>28</sup> and 91% versus 90%<sup>26</sup> versus 82%<sup>28</sup>), demonstrating robustness of the method also in a European multicenter setting. The added benefit of 3D myocardial perfusion CMR over 2D three-slice imaging for assessing MIB has recently been indicated.<sup>27</sup> Furthermore, the high interstudy, intra- and inter-reader reproducibility has been confirmed.<sup>18,28</sup> Although the present multicenter study was conducted using 3.0 T CMR systems, the protocol is readily applicable to 1.5 T machines as demonstrated previously.<sup>28</sup> Application of the method on MR systems from different vendors is possible upon modification of the pulse sequence and image reconstruction software. To this end, the image reconstruction code is provided on request.

Although previous single-center validation of 3-slice 2D approaches using 1.5 T CMR systems yielded similarly high sensitivity and specificity relative to FFR,<sup>16</sup> the assessment of ischemic tissue volume was not possible given the limited coverage of 2D methods. As demonstrated previously, the diagnostic performance of 3D perfusion imaging compares favorably against simulated 3-slice data extracted from the 3D volume.<sup>18,26</sup>

According to current guidelines, the decision to perform coronary revascularization procedures should be based on an objective documentation of myocardial ischemia preferably together with its anatomic localization and amount.<sup>17</sup>

Based on current and previous studies, 3D myocardial perfusion CMR may prove a valuable alternative to methods using ionizing radiation to monitor and guide treatment. CMR also allows imaging of at least the proximal coronary anatomy and fusion of 3D CMR perfusion with coronary CMR or low-dose coronary computed tomography angiography

(CCTA) offering promise for future comprehensive noninvasive assessment of CAD.<sup>33</sup>

The amount of myocardial ischemia is a key factor to guide treatment decisions, that is, revascularization is recommended in case MIB exceeds 10%<sup>30</sup> of total left ventricular myocardium. However, these cut-off values were derived from nuclear studies<sup>34,35</sup> and, although never directly compared, may not apply to 2D perfusion CMR in view of its limited cardiac coverage. Three-dimensional myocardial perfusion CMR and single photon emission computed tomography agree well with the 10% threshold,<sup>27</sup> highlighting another potential benefit of 3D whole-heart versus 2D multislice myocardial perfusion CMR.

Today, the invasive assessment of the functional significance of coronary lesions is the basis of therapeutic decision-making,<sup>36,37</sup> even though FFR measurements are invasive, time-consuming, and associated with radiation exposure rendering the method less attractive for monitoring patients. To this end and based on the evidence presented here and elsewhere, 3D myocardial perfusion CMR may be considered a noninvasive alternative to stratify patients according to guidelines.

### Study Limitations

An important limitation of the study design is that only patients who were already scheduled for a coronary angiogram were recruited in the study. This fact reflects the current practice of referral by external physicians. In line with current guidelines and to minimize complications of FFR measurements, hemodynamic assessments were only performed in vessels with luminal stenosis of 50% to 80% at angiography. In addition, the assessment of MIB was given as percentage ischemic myocardium, reflecting only relative myocardial perfusion distribution at one particular time point during the dynamic first-pass of the contrast agent. Accordingly, MIB is not a direct measure of quantitative myocardial blood flow. It is furthermore acknowledged that all CMR centers involved in our study are specialized in CMR imaging, and it remains to be demonstrated how the technique performs at sites with less experience and expertise.

### Conclusions

This multicenter study has demonstrated the robustness and accuracy of 3D myocardial perfusion CMR to detect functionally significant CAD as measured by FFR.

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### Disclosures

T.F. Luescher has received consulting honoraria from Philips Healthcare. The other authors report no conflicts.

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### CLINICAL PERSPECTIVE

Cardiovascular MRI (CMR) is increasingly established as an important method for the diagnosis of cardiovascular disease. First-pass myocardial perfusion CMR imaging yields high diagnostic accuracy for the detection of coronary artery disease. However, standard 2D multislice CMR perfusion techniques provide only limited cardiac coverage and hence considerable assumptions are required to assess myocardial ischemic burden. To address the limited coverage of 2D multislice myocardial perfusion CMR techniques, three-dimensional (3D) methods have been developed based on recent advances in CMR scan acceleration methodology. Using a multicenter setting, dynamic 3D-CMR stress perfusion imaging is shown to provide high diagnostic accuracy and allows quantification of the percentage of ischemic myocardium by direct volumetry. Because measurements of ischemic burden are increasingly used to guide decision-making regarding the need for revascularization with >10% ischemic burden, 3D-CMR perfusion imaging is expected to play an important role as a noninvasive and radiation-free method for stratifying patients with stable coronary artery disease.



## Multicenter Evaluation of Dynamic Three-Dimensional Magnetic Resonance Myocardial Perfusion Imaging for the Detection of Coronary Artery Disease Defined by Fractional Flow Reserve

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